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Fusion PET–CT imaging of neurolymphomatosis

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In a patient suffering from peripheral neuropathy due to neurolymphomatosis, fused PET–CT imaging, performed on a novel in-line PET–CT system, showed multiple small nodular lesions extending along the peripheral nerves corresponding to an early relapse of a transformed B-cell non-Hodgkin's lymphoma.

Key words: fusion PET–CT imaging, neurolymphomatosis, non-Hodgkin's lymphoma, peripheral neuropathy

Introduction

Non-Hodgkin's lymphoma involving the peripheral nervous system is a rare cause of peripheral neuropathy. The differential diagnosis comprises herpes zoster infection, vinca alkaloid toxicity, compression or infiltration of nerve roots, lymphoma-associated vasculitis and systemic amyloidosis [1]. In the present case we demonstrate that co-registered imaging with positron-emission tomography (PET) and computed tomography (CT), in a novel in-line PET–CT scanner, represents a valuable method to visualize peripheral nerve involvement in an early relapsed aggressive non-Hodgkin's lymphoma.

Case report

A 65-year-old woman was admitted to the hospital because of progressive motor and sensory impairment in her right arm. Nine years previously, the patient had undergone radiotherapy (36 Gy) for a stage IA follicular B-cell non-Hodgkin's lymphoma in the left lower pelvis. Thereafter, the patient remained in complete remission. Eight months ago, the woman was admitted to the hospital for abdominal discomfort associated with increasing weakness of the right leg over a course of 3 months. On physical examination, a large mass was noted in the right abdomen and edema of the lower right extremity. Lactate dehydrogenase was 1880 U/l (<540) and no pathological protein was detected in the serum immune electrophoresis. A CT scan of the abdomen and pelvis showed a large abdominal/pelvic mass (18 × 18 × 12 cm); the histopathological examination of a biopsy revealed a diffuse large B-cell non-Hodgkin's lymphoma. No hepatosplenomegaly, lymphadenopathy or bone marrow infiltration were found.

The weakness of the right leg was due to an obturator mono-neuropathy. After six cycles of CHOP chemotherapy (cyclophosphamide, doxorubicin, vincristine, prednisone), magnetic resonance imaging (MRI) revealed no residual tumor. However, the weakness of the right leg improved only slightly.

Two weeks after the last systemic chemotherapeutic cycle, the patient complained of painful sensations and progressive weakness in the extensors of the fingers of the right hand. A neurologic examination revealed the beginnings of atrophy in all the small muscles of the right hand. An electromyographic examination showed a small median-nerve compound muscle action-potential with delayed distal motor latency. The ulnar-sensory and motor-nerve conduction signals were pathological with high spontaneous activity potentials, consistent with a severe proximal axonal sensorimotor neuropathy of the ulnar and median nerve. The fusion of PET and CT scans showed a number of small lesions along the plexus brachialis and vessel-nerve bundle of the right arm (Figures 1 and 2). Due to the rapid progression of neurologic symptoms, percutaneous radiotherapy was performed involving the right axillary and brachial region (total 40 Gy). However, the patient's disease progressed rapidly with an extensive increase in 2-[F-18]-fluoro-2-deoxy-D-glucose (FDG) uptake in the right upper arm and both axillary regions (Figures 3 and 4). After two cycles of salvage therapy (rituximab-ifosfamide, cytarabin, etoposide) the lymphoma showed impressive clinical regression. However, no recovery of the associated neuropathy could be observed. After four cycles of salvage chemotherapy the combined PET–CT showed complete regression of all lymphoma manifestations. Unfortunately, the associated neuropathy of the right arm persisted.

Materials and methods

A fusion of PET and CT scans was performed on an in-line PET–CT system to confirm the hypothesis that the early relapse of the lymphoma with extension along the peripheral nerves was underlying the peripheral

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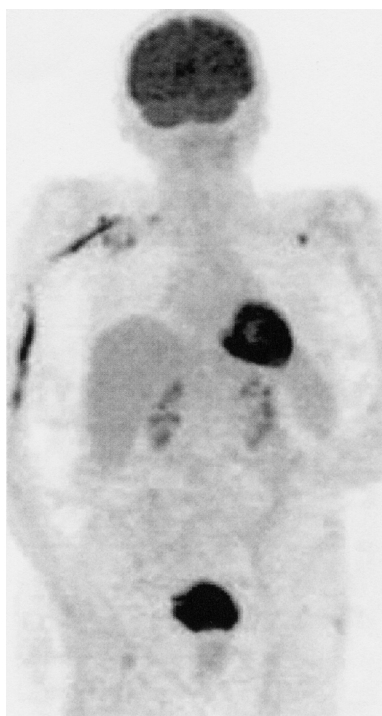
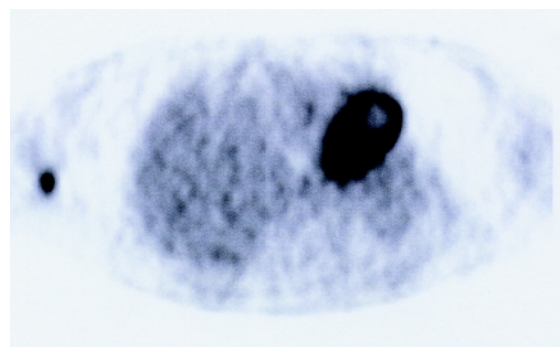


Figure 1. Maximum intensity projection PET image showing a contiguous lesion along the plexus brachialis and the vessel-nerve bundle of the right arm. A second lesion is seen in the left axillary region.

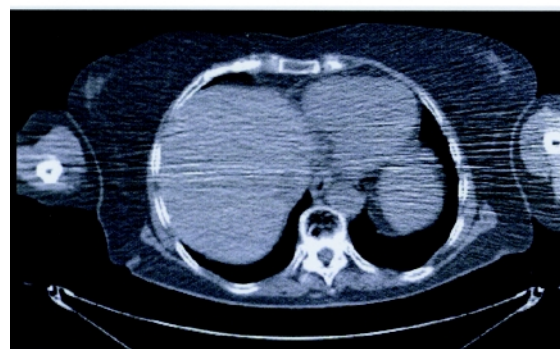
neuropathy. Imaging and data acquisition was performed on a novel combined PET–CT in-line system (Discovery LS; GE Medical Systems, Waukesha, WI, USA), combining the ability to acquire CT images and PET data from the same patient in one session. A GE Advance NXi PET scanner and a multislice helical CT (LightSpeed plus) were integrated in this dedicated system. The axes of both systems were mechanically aligned to coincide perfectly. Sixty to 120 min after i.v. injection of 10 mCi of FDG, emission data were acquired at six incremental table positions, each 146 mm wide, thereby covering 867 mm of table travel. For each position, 35 two-dimensional non-attenuation-corrected scans were obtained simultaneously over a 4 min period. CT data were used for attenuation correction. Therefore, data acquisition was performed within 25 min to cover from the skull-base to the level of the pelvic floor. Viewing of co-registered images was performed with dedicated software (eNTEGRA, ELGEMS, Haifa, Israel).

Discussion

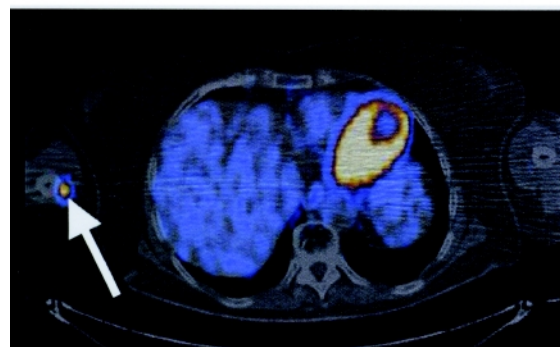
Peripheral nervous system involvement of lymphoma is rare. Experience with lymphoma presenting as a solitary tumor of a peripheral nerve and the dissemination of lymphoma extending along peripheral nerves is limited to few case reports [2, 3]. The clinicopathologic syndrome of neurolymphomatosis (NL), or lymphomatous infiltration of peripheral nerves, is a relatively rare condition that usually develops in patients with widespread non-Hodgkin's lymphoma and may be the first manifestation or the sole relapse site [4, 5]. Neurolymphomatosis-related painful polyneuropathy has been



A



B



C

Figure 2. (A) PET image indicating increased FDG uptake in the medial aspect of the arm and enhancement of the heart. (B) Non-enhanced CT scans at the same level showing no evidence of a tumor. (C) PET–CT fusion shows clear localization of the lesion within the neurovascular bundle of the right arm (arrow).

described during or immediately after a course of systemic chemotherapy and despite a good response of the systemic disease [5], similar to the clinical presentation in our patient.

Differential diagnoses include reactivation of latent herpes zoster virus, which usually shows a dermatomal distribution associated with severe pain, but which may also lead to systemic manifestation [6]. Furthermore vinca alkaloids, which are commonly used drugs in lymphoma treatment, as well as radiation plexopathy, may cause peripheral neuropathy [7]. Lymphoma-associated vasculitis and systemic amyloidosis

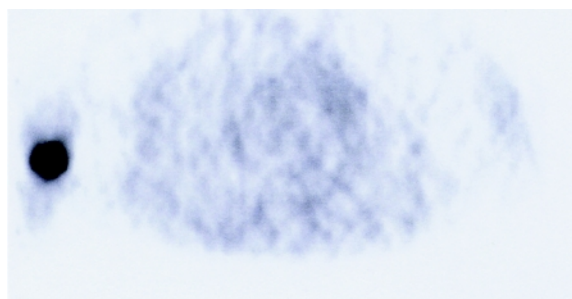


Figure 3. Maximum intensity projection PET image from the follow-up examination, revealing an extensive increase in the tumor burden in the right arm and new lesions in the left side.

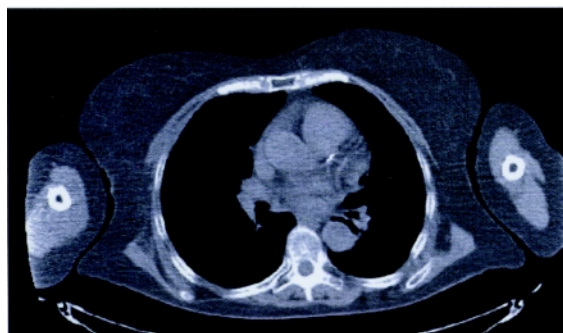
may present with peripheral neuropathy and can be difficult to distinguish from nerve root compression or multifocal neoplastic infiltration [1, 8–10].

In patients with Morbus Hodgkin and, as recently described, non-Hodgkin's lymphoma, who develop neurological symptoms, Guillain-Barré syndrome should also be considered in the differential diagnosis [11]. Diagnosis of NL usually requires histologic demonstration of infiltrating malignant lymphocytes in a peripheral nerve. However, nerve biopsy may fail despite the widespread lymphomatous infiltration of peripheral nerves [5]. While MRI can be useful in identifying affected nerves, it may not be sensitive enough for small lesions [12, 13]. The role of PET in the assessment of non-Hodgkin's lymphoma and as a prognostic marker is under evaluation. Recent reports show encouraging results, especially in follow-up examinations after chemotherapy [14–18].

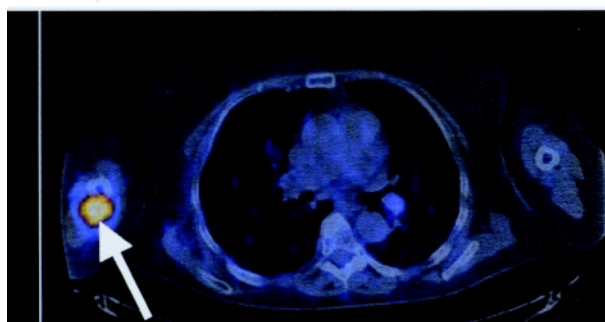
During the early years of clinical tumor imaging with PET the potential of multi-modality image fusion has been recognized [19]. Meanwhile, several studies have shown that a combination of PET and CT by software co-registration is more accurate than CT alone, especially in staging non-small-cell lung cancer and detection of mediastinal lymph node metastases [20]. Recently, Townsend et al. [21] introduced a combined PET-CT scanner, using a low performance helical CT and a low performance PET scanner, which permits the acquisition of co-registered PET and CT images in the same imaging session. Analysis of the results showed an improvement in lesion localization and classification. The technique



A



B



C

Figure 4. (A) Axial PET image at the level of the right arm showing an increase in FDG uptake in the right arm. (B) In this CT image, a mass is seen in the neurovascular bundle, which corresponds to the FDG uptake as proven by (C) the fused PET-CT image (arrow).

used in this case is more advanced since high-end PET and CT scanners were involved, which allowed for rapid data acquisition in <30 min. An advantage lies in the higher confidence level of lesion localization that fusion PET-CT may provide. However, this technique is limited by the nature of FDG uptake, since inflammatory lesions may show an increased accumulation of the tracer as well. In this case, inflammatory changes can be excluded by the clinical course of the disease.

In conclusion, causes of peripheral neuropathy may be difficult to distinguish during progressive disease and therapy of aggressive lymphoma. The fusion of PET and CT data may provide a novel tool for imaging NL in relapse of aggressive

non-Hodgkin's lymphoma and prompt therapeutic implications without the risk of invasive manoeuvres.

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